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10/696,572	10/30/2003	Masataka Andoh	016778-0470	5923

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EXAMINER	
DEJONG, ERIC S	

ART UNIT	PAPER NUMBER
1631	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/696,572	ANDOH ET AL.	
	Examiner	Art Unit	
	ERIC S. DEJONG	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 July 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,7-17,19-25 and 27-34* is/are pending in the application.

4a) Of the above claim(s) *4,16,29,30 and 32-34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5,7-15,17,19-25,27,28 and 31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED OFFICE ACTION

Applicants response filed 07/24/2008 is acknowledged.

Claims 6, 18 and 26 are cancelled. Claims 1-5, 7-17, 19-25, and 27-34 are pending. Claims 4, 16, 29, 30, and 32-34 are withdrawn as being drawn to a non-elected species (see applicants response filed 05/16/2006 and page 2 of the Office action mailed 09/15/2006). Claims 1-3, 5, 7-15, 17, 19-25, 27, 28, and 31 are currently under examination.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 101

The rejection of claims 1-3, 5, 7-15, 17, 19-25, 27, 28, and 31 under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter is withdrawn in view of amendments made to the instant claims.

In regards to the previous rejection of claim 27 under 35 USC 101 as being directed to non-statutory subject matter, applicants argue that page 14 of the instant specification defines "computer readable medium" as being limited only to physical media. Applicants argument has been accepted as an estoppel on the record that the instant claims were never intended to read on signal or carrier wave embodiments.

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-3, 5, 7-15, 17, 19-25, 27, 28, and 31 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The following rejection is newly applied.

The recent en banc decision regarding Bilski v. Warsaw (2008) set forth that a process is patent-eligible if (1) it is ties to a particular machine or apparatus or (2) it transforms a particular article into a different state or thing.

The instant claims are drawn to a method and related computer apparatus and program for the correction of microarray data. The claimed process, which is further carried out by said computer related apparatus and program, involves the abstract and computational steps of inputting gene expression intensity data, standardizing said gene expression intensity data, outputting said standardizing gene expression intensity data, estimating distortion, outputting a first corrected gene expression intensity data, performing an S-D transformation of said data, and outputting a second corrected gene intensity data. The instant claims do not recite or inherently involve any transformation of a particular article, therefore the Examiner must determine if the instant claims have a tie to a particular machine or apparatus. Instant claims 13-15, 17, 19-25, and 31 do not recite any limitation directed to a particular apparatus. The recitation of an output to a display in said claims has been treated as insignificant post solution activity as the display is not involved in the steps directed toward the correction of micrroarray data. Further, both the apparatus and computer readable embodiments as set forth in claims

1-3, 5, 7-12, 27, and 28 serve only as general purpose computing means that perform the method as set forth above, and as such wholly preempt an abstract process. Therefore, the instant claims are directed towards non-statutory subject matter.

Claim Rejections - 35 USC § 112, Second Paragraph

The previous rejection of claim 5 under 35 USC 112, second paragraph, for lack of antecedent basis is withdrawn in view of arguments presented by applicants.

The previous rejection of claims 11, 12, and 23-25 under 35 USC 112, second paragraph, as being indefinite regarding the recitation of the limitation "the correction" in line 3 of said claim is withdrawn in view of amendment made to the instant claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3, 5, and 7-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Independent claim 1 recites a series of means plus function language in the limitations "a data standardization means for standardizing the gene expression intensity data" (see lines 8-10 of claim 1), "first correction means for estimating distortion" (see lines 11-14 of claim 1), "second correction means for performing an SD transformation" (see lines 15-20 of claim 1). Similarly, Claim 2 recites the limitation of "S-D transformation means for quantifying the distortion of the gene expression

intensity" (see lines 2 and 3 of claim 2). The recitation of means plus function language in a claim invokes 35 U.S.C. 112, sixth paragraph in order to determine the metes and bounds of the claimed invention. Regarding the use of means plus function limitations in a claim, MPEP §2181(II) states:

> "35 U.S.C. 112, sixth paragraph states that a claim limitation expressed in means-plus- function language "shall be construed to cover the corresponding structure…described in the specification and equivalents thereof." "If one employs means plus function language in a claim, one must set forth in the specification an adequate disclosure showing what is meant by that language. If an applicant fails to set forth an adequate disclosure, the applicant has in effect failed to particularly point out and distinctly claim the invention as required by the second paragraph of section 112." In re Donaldson Co., 16 F.3d 1189, 1195, 29 USPQ2d 1845, 1850 (Fed. Cir. 1994) (in banc)."

Upon review, the instant disclosure is inadequate as it fails specify any structure corresponding to the means as recited in the instant claims. It is further noted that the recent CAFC decision in *Biomedino v. Waters Technology* (Fed. Cir. 2007) held that the structure of a claimed "means" must be expressly disclosed in the specification even if one of skill in the art could implement a structure without such a disclosure. Therefore, the recited "means" causes the metes and bounds of the instant claims to be indefinite because there is no corresponding disclosure of what structures are specifically encompassed by said means. Claims 2, 3, and 5-12 are also included under this rejection due to their dependence from claim 1.

Response to Arguments

Applicant's arguments filed 07/24/2008 have been fully considered but they are not persuasive.

In regards to the rejection of claims 1-3, 5, and 7-12 under 35 U.S.C. 112, second paragraph, as being indefinite, applicants argue that page 9 and Figure 2 of the

instant specification describes a "data standardization unit", a "spot-position-based correction unit, and a "S-D-plot-based correction unit" which correspond to the recited means.

In response, it reiterated that although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). The means as recited in the instant claims are much broader in scope than the units identified by applicants. Further, the instant claims do not recite the limitations of a "data standardization unit", a "spot-position-based correction unit, and a "S-D-plot-based correction unit". The basis of the instant rejection is that the structure the specified means is not defined by the instant specification, but rather their described only by their function. It is maintained that the instant specification fails to sufficiently describe the structure corresponding to the means as recited in the instant claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 2, 13-14, and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yang et al. (Nucleic Acids Research, 2002, Vol. 30, pages 1-10) in view of Weng (US PGPUB 2003/0226098).

Claim 1 is drawn a cDNA microarray data correction system for correcting global an local distortions of microarray data and correcting measurement errors caused by a difference in sensitivity between fluorescent dyes comprising five steps.

The preamble of claim 1 is taught in the first two sentences of the abstract of Yang et al. which states:

> There are many sources of systematic variation in cDNA microarray experiments which affect the measured gene expression levels (e.g. differences in labeling efficiency between the two fluorescent dyes). The term normalization refers to the process of removing such variation.

The first step of the body of instant claim 1 states gene expression intensity data is input and background noise is removed. The passage under “Image processing” in column 2 of page 2 of Yang et al. states:

> Each hybridization produced a pair of 16-bit images, which were processed using the software package Spot. The main quantities of interest produced by the image analysis methods (segmentation and background correction) are the (R,G) fluorescence intensity pairs for each gene on each array (where R = red for Cy5 and G = green for Cy3). Note that we call the spotted DNA sequences ‘genes,’ whether they correspond to actual genes, ESTs or DNA sequences from other sources.

The second step of data standardization using grid-by-grid order statistics for inputting and transmitting gene expression data is described at the top of page 3, column 1 of Yang et al., which is entitled, “Within-print tip group normalization” and is based in part on grid data. The model listed is used to input and transmit data.

The third step of instant claim 1 is a first correction means for performing a distortion depending or a spot position on grid coordinates for the standardized gene expression intensity data. The "Scale normalization" section in column 1 (line 8) of page 3 of Yang et al. teaches such a normalization. The equations in this section illustrate a nonparametric smoothing method.

The fourth step of instant claim 1 is a second correction means for performing a distortion depending or a spot position on grid coordinates for the standardized gene expression intensity data. The "Composite normalization" section in column 1 (line 8) of page 3 of Yang et al. teaches such a second correction means. In addition, the "Intensity-dependent normalization" at the bottom 10 lines of column 2 of page 2 of Yang et al. describes the use of MA plots (i.e. output) and could also serve as a second correction means for the data.

The instant claims have further been amended to recite "wherein the standardized gene expression intensity data is represented by a sum of a true gene intensity and distortion depending on the spot. While not expressly taught by Yang et al., the resultant gene expression intensity data as recited in the instant claim reads only on a reorganization of data, per se, and does not serve to produce any new or useful information beyond that which was already present and apparent to one having ordinary skill in the art. As such, the reorganization of data as instantly claimed fails to differentiate the instant claims from the processes and devices as set forth in the prior art.

However, the article of Yang et al. does not teach S-D transformations.

The application of Weng, entitled "Methods for analysis of measurement errors in measured signals" performs second derivative transformations to analyze microarray data (see paragraphs [0064] to [0070]). The purpose of the application of Weng is described in paragraph [0010] which states:

> The present invention provides methods for analyzing measurement errors in measured signals obtained in an experiment, e.g. measured intensity signals obtained in a microarray gene expression experiment or microarray proteomics experiment. Signals from any experimental measurement can be analyzed by the methods of the present invention.

It would be obvious for someone of ordinary skill in the art at the time of the instant invention to modify the microarray normalization methods of Yang et al. by use of the microarray signal transformations of Weng because while Yang et al. transforms and plots the experimental data according to the theories proposed, Weng has the advantage of using the required S-D (second derivative) transformation for the ability to better analyze microarray signal data.

Related transformations are plotted in the Figures 1-4 of Weng (the additional limitation of instant claim 2 is a plot of the S-D transformation).

It would be obvious for someone of ordinary skill in the art at the time of the instant invention to modify the microarray normalization methods of Yang et al. by use of the microarray signal transformations of Weng because while Yang et al. transforms and plots the experimental data according to the theories proposed, Weng has the advantage of using the required S-D (second derivative) transformation for the ability to better plot error in microarray signal data.

Instant claim 13 is drawn to a species of instant claim 1 with several intermediate outputting steps after each transformation.

It would have been obvious to someone of ordinary skill in the art to repetitively output results of each intermediate transformation because it is obvious to repeat the steps of a claim. In this instance, instant claim 1 outputs results as a final step. It is obvious to repeat this step of outputting the results at various points in the claim because there is no mandating of the order in which to carry out the steps of instant claim 1. In other words, instant claim 1 can be repeated multiple times with the outputting steps at each of the same locations of the outputting steps in instant claim 13 and make obvious instant claim 13 over the prior art used for instant claim 1.

Related transformations are plotted in the Figures 1-4 of Weng (the additional limitation of instant claim 14 is a plot of the S-D transformation).

It would be obvious for someone of ordinary skill in the art at the time of the instant invention to modify the microarray normalization methods of Yang et al. by use of the microarray signal transformations of Weng because while Yang et al. transforms and plots the experimental data according to the theories proposed, Weng has the advantage of using the required S-D (second derivative) transformation for the ability to better plot microarray signal data error.

Instant claim 27 is drawn to the same method steps as instant claim 13 with the additional limitations of claims 27 having preambles indicating the method is a DNA microarray data correction program, and a computer readable medium containing the DNA microarray data correction program, respectively.

Weng discloses a computer with computer readable media in Figure 14.

It would be obvious to someone of ordinary skill in the art at the time of the instant invention to modify Yang et al. in view of the automated method of Weng because Weng can carry out the method expeditiously and accurately on a computer system.

Response to Arguments

Applicant's arguments filed 07/24/2008 have been fully considered but they are not persuasive.

In regard to the rejection of claims under 35 USC 103(a) as being unpatentable over Yang et al. in view of Weng, applicants argue that the instant claims have been amended to recite "wherein the standardized gene expression intensity data is represented by a sum of a true gene intensity and distortion depending on the spot.

In response, it is reiterated from the instant rejection that the resultant gene expression intensity data as recited in the instant claim reads only on a reorganization of data, per se, and does not serve to produce any new or useful information beyond that which was already present and apparent to one having ordinary skill in the art. As such, the reorganization of data as instantly claimed fails to differentiate the instant claims from the processes and devices as set forth in the prior art.

Applicants further reiterate the previous argument that one of ordinary skill in the art would recognize that no consideration is made at all in Yang et al. about a distortion

dependent upon the coordinate positions between grids and that such a distortion dependent on the coordinate position is never corrected in Yang et al.

In response to applicant's arguments against the references individually, it is first noted that one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Further, it is reiterated that the "Composite normalization" section in column 1 (line 8) of page 3 of Yang et al. teaches such a second reads on the recited means and step for performing a distortion depending or a spot position on grid coordinates for the standardized gene expression intensity data. This section of Yang et al. expressly addresses the normalization of data collected from different print tip groups which read on coordinate positions between grids as instantly claimed. Therefore, the rejection of claims 1, 2, 13-14, and 26-27 under 35 U.S.C. 103(a) as being unpatentable over Yang et al. in view of Weng is maintained.

Applicants further reiterate the argument that the references do not provide any suggestion or motivation that would lead one skilled in the art to combine Yang et al. and Weng to arrive at the presently claimed invention.

In response, it is reiterated that in the recent Supreme Court decision in *KSR International Co. v. Teleflex Inc.* expressly rejected the application of a rigid TSM test in determining obviousness. Further, the court ruled that "(t)he combination of familiar elements according to known methods is likely to be obvious when it does no more than

yield predictable results". In the instant case, one of ordinary skill in the art would recognize that the combination of teachings set forth by Yang et al. and Weng would yield predictable results. Further, applicants have not demonstrated or presented arguments as to why the results produced by the instant claims would be unexpected or unpredictable beyond that which is taught in the prior art. Therefore, the rejection of claims under 35 U.S.C. 103(a) as being unpatentable over Yang et al. in view of Weng is maintained.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ERIC S. DEJONG whose telephone number is (571)272-6099. The examiner can normally be reached on 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran can be reached on (571) 272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a

USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Eric S DeJong/
Primary Examiner, Art Unit 1631